concentrated, phytoestrogen-derived isoflavones selected from the group consisting of Genistein, Daidzein, Biochanin A, Formonoetin or the natural glycosides of any of said phytoestrogens.

11 12
~~10~~ ~~11~~. A pharmaceutical preparation, as claimed in claim ~~36~~, wherein said solid dosage unit is selected from the group consisting of a pill, tablet, coated tablet, capsule or powder.

13
~~38~~. A pharmaceutical preparation, as claimed in claim ~~37~~, wherein said isoflavone is present in said solid dosage unit in an amount from about 20 mg. to about 200 mg. per dosage unit.

Cancel claims ~~1~~, ~~4~~, ~~10~~, ~~11~~, ~~18-20~~ and ~~23-28~~.

REMARKS

The September 10, 1996 Official Action and the references cited therein have been carefully considered. In view of the amendments presented herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

In the September 10 Official Action, a formal objection has been raised under 37 C.F.R. §1.72(b), and an abstract on a separate sheet is required.

Also in the September 10 Official Action, the specification has been objected to, and claims 1-28 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to adequately teach how to make and use the claimed invention. The reasons on which these related grounds of objection and rejection are premised appear at pages 2-10 of the Official Action. These reasons include a lengthy discussion of the so-called "Forman factors" in support of the contention that undue experimentation would be required on the part of those skilled in the art in order to practice the

claimed invention. According to the Examiner, the amount of experimentation needed to verify the efficacy of the potential compositions for inclusion in a health supplement would be voluminous and unduly burdensome in view of the teachings of the instant disclosure.

Claims 1-9, 21 and 22 also stand rejected under 35 U.S.C. §103 as allegedly unpatentable in view of the disclosure of U.S. Patent 4,366,082 to Zilliken. According to the Examiner, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include one or more phyto-oestrogen compounds into a composition to improve the health of the recipient, because the prior art discloses the inclusion of this class of compounds generically into compositions to be used as anti-oxidants.

Applicant, through his undersigned attorney, requested a personal interview with Examiner Wilson, which was held on February 19, 1997. The courtesy extended to applicant and his representatives in granting the interview is appreciated. The purpose of the interview was primarily to present an overview of the invention, as well as evidence as set forth in the Declaration of Dr. Kelly submitted herewith, which applicant believes clearly refutes the premise on which the §112, first paragraph, rejection is based. Certain amendatory language was discussed in connection with the broad composition and method claims, which the Examiner recommended that the applicant consider as a way of overcoming the §112, first paragraph, rejection of record.

At the conclusion of the interview, it was indicated that appropriate claim amendments would be presented to satisfy the requirements of 35 U.S.C. §112, first paragraph. The substance of the interview is fairly set forth in the Examiner Interview Summary Record (PTOL-413) in the official application file.

In accordance with the present amendment, the specification has been amended to include an abstract on a single sheet as required under 37 C.F.R. §1.72(b).

Turning to the present claim amendments, claim 1 has been rewritten as claim 29, which is directed to a health supplement composition comprising an extract from soya or clover, the composition comprising any two or more phyto-oestrogens selected from the group consisting of Genistein, Daidzein, Biochanin A, Formononetin or the natural glycosides of any of said phyto-oestrogens. Claim 10 has also been rewritten as new claim 30, which is drawn to a method for treating or reducing the predisposition to a condition selected from the group consisting of benign breast disease, premenstrual syndrome (PMS), symptoms associated with menopause, cancer of the prostate, or elevated blood cholesterol, said method comprising administering to a subject having said condition or predisposed to said condition a therapeutically effective amount of a health supplement composition comprising an extract from soya or clover, said composition comprising any two or more phyto-estrogens of the group Genistein, Daidzein, Biochanin A, Formonoetin or the natural glycosides of any of said phyto-estrogens.

New claims 31-35 are directed to the treatment and/or prevention of the following specific conditions: (i) elevated levels of cholesterol in the blood stream; (ii) cancer of the prostate; (iii) pre-menstrual syndrome; (iv) symptoms associated with menopause; and (v) benign breast disease. New claims 36-38 are directed to a particularly preferred embodiment of the invention which was discussed at the February 19, 1997 interview. Support for new claims 36-38 is provided in the present specification at page 13, line 26 through page 14, line 7 and page 16, lines 7-12.

The language of new claim 30 varies somewhat from the language discussed at the February 19 interview, because on further review it was found that the specification does not have verbatim support for the recitation "clinically predisposed". As set forth in new claim 30, the recitation "or prevention" has been deleted, as discussed at the interview, and replaced with "reducing the predisposition to"

(see page 7, line 15 of the present specification), and the recitation "at risk" has been changed to read "predisposed to said condition", which is believed to been in keeping with the substance of what was discussed at the interview. This departure from the claim language discussed at the interview was undertaken for the sake of conformity between new claim 30 and the description of the invention provided in the specification.

The present amendments further define the composition of the invention, as well as conditions described in the specification that are treatable with the composition of the invention. Support for the compositions containing extracts of soya or clover is specifically provided, for example, at pages 11 and 12 and in Examples 1 and 2 at pages 17 through 19.

The recitation of "improving the health of a human" has been omitted from the amended claims presented herewith.

No new matter has been introduced into this application by reason of these amendments.

In view of the foregoing amendments, the objection to the specification and related rejection of claims 1-28 under 35 U.S.C. §112, first paragraph, based on alleged inadequate enablement, and the 35 U.S.C. §103 rejection of claims 1-9, 21 and 22 based on the Zilliken patent are respectfully traversed.

1. As Presently Amended, Applicant's Claims Fully Comply with the Enablement Requirement of 35 U.S.C. §112, First Paragraph

Initially, it is noted that at page 3 of the September 10, 1996 Official Action, the Examiner acknowledges the sufficiency of applicant's disclosure with regard to lowering of cholesterol levels. That being the case, the objection/rejection under §112, first paragraph, is clearly inapplicable to new claim 31.

Addressing the "how to make" requirement of 35 U.S.C. §112, first paragraph, methodology for obtaining the active agents of the present invention, namely, Genistein,

Daidzein, Biochanin A, Formononetin or the natural glycosides of such phyto-oestrogens is described in detail at pages 11-13 of the present specification and exemplified in Example 1 (derivation from red clover) and Example 2 (derivation from soy beans), at pages 17-19 of the present specification. These examples produce compositions from clover and soy which are not limited only to Genistein and Daidzein, or to any specific ratio of the active agents.

Turning to the "how to use" requirement of §112, first paragraph, the pharmaceutically effective amounts of the composition are described in detail at page 14 of the specification and specifically exemplified in Examples 3 and 4. Example 3 describes the beneficial therapeutic effect of administering red clover extract to humans which is manifested in a lowering of total serum cholesterol levels, without producing any undesirable side effects. Example 4 describes the beneficial therapeutic effect of administering soy hypocotyls which is manifested in both lower cholesterol levels and amelioration of benign breast disease. Furthermore, these examples show therapeutic treatment wherein the composition of the invention is administered in an amount of 100 mg. (Example 3) and 50 mg. (Example 4) on a daily basis.

As for the additional conditions specified in the newly added claims, there is submitted herewith a Declaration of Graham Edmund Kelly, the inventor herein, which establishes that treatments conducted at his request or under his supervision, in accordance with this invention, were shown to be effective with respect to (i) prostate cancer; (ii) benign or cystic breast disease; (iii) pre-menstrual tension; and (iv) symptoms of menopause.

The Declaration of Dr. Kelly further shows that therapeutic effectiveness is evidenced when the compositions of the invention are administered in varying amounts from 40 mg to 240 mg of phyto-oestrogen, most of which are within the range described at page 14 of the present specification as the

preferred dosage amounts, and all of which are within the range disclosed as operable.

The Declaration of Dr. Kelly submitted herewith is an unsigned copy of the same Declaration that was reviewed at the February 19 interview. A signed copy of Dr. Kelly's Declaration will be submitted in a supplemental response to the September 10, 1996 Official Action.

The Declaration of Dr. Kelly provides clear evidence demonstrating that the scope of enablement provided by the present specification is fully commensurate with the scope of patent protection sought by the amended claims. Such declaration evidence is properly presented in rebutting an allegation of inadequate enablement under 35 U.S.C. §112, first paragraph. *In re Armbruster*, 185 U.S.P.Q. 152 (CCPA 1975). As was the case in *Armbruster*, the Declaration of Dr. Kelly is being submitted only to demonstrate that the teaching in the specification is adequately enabling.

In summary, the pharmaceutically effective amounts of the compositions are described specifically at page 14 of the present specification and more particularly exemplified in Examples 3 and 4. Moreover, the therapeutic treatment set forth in Dr. Kelly's declaration fully support the dosage ranges referred to at page 14. The present specification provides an enabling description of the lowering of cholesterol levels and the treatment of benign breast disease in Examples 3 and 4. The Declaration of Dr. Kelly specifically demonstrates the treatment of the additional conditions which are specifically claimed in the amendments presented herewith, namely, the treatment of prostate cancer, benign or cystic breast disease, premenstrual syndrome and symptoms associated with menopause.

For all of the foregoing reasons, the objection to the specification and related rejection of claims 1-28 under 35 U.S.C. §112, first paragraph, is untenable and should be withdrawn.

2. **The Disclosure of Zilliken Does Not Render Obvious the Subject Matter of Claims 1-9, 21 and 22**

As noted by the Board of Appeals in *Ex Parte Wolters*, 214 U.S.P.Q. 735 (Bd. Apps. 1979), the burden of establishing a *prima facie* case of obviousness falls upon the Examiner. In determining whether a case of *prima facie* obviousness exists, it is necessary to ascertain whether or not the disclosure of the cited prior art would appear to be sufficient to one of ordinary skill in the art to make the substitution, combination or other modification required to arrive at the claimed subject matter. *In re Lalu*, 223 U.S.P.Q. 1257 (Fed. Cir. 1984). In the present case, there is nothing to suggest the modification of the compounds disclosed in the Zilliken patent which is required to arrive at the composition claimed by applicant herein.

The Zilliken patent purports to disclose a class of isoflavone derivatives recoverable from a substance known as "temph", which possess anti-oxidant properties. The utility disclosed for these isoflavone derivatives is in the "stabilization of a wide variety of food products including edible fats and oils" (see column 2, lines 20-22).

All of the isoflavone derivatives disclosed in the Zilliken patent as possessing anti-oxidant properties have an -OR substituent in the 6-position of the structural formula, wherein R may be a methyl, ethyl or hydrogen substituent, as described at columns 2 and 3 of the Zilliken patent. The active agent incorporated in the compositions of the present invention, by contrast, are unsubstituted in the 6-position. See the structural formula set out at page 9 of the present specification.

Although the Zilliken patent acknowledges that Genistein and Daidzein are recoverable from temph, there is no clear disclosure that Genistein and Daidzein possess anti-oxidant properties, or indeed are within the ambit of the invention described and claimed in the Zilliken patent. On

the contrary, a review of the Zilliken patent claims plainly reveals that Genistein and Daidzein are outside the scope of the claimed invention for the reasons stated above, i.e., all of the isoflavone derivatives identified as having the desired anti-oxidant properties include a substituent in the 6-position of the claimed structural formula.

Thus, the evidence of alleged obviousness in this case fails to show or suggest the removal of the -OR substituent from the isoflavone derivatives disclosed in the Zilliken patent, which is required to arrive at the compounds included in the compositions of the present invention. In the absence of such showing or suggestion, there is inadequate support for the Examiner's position that the compositions claimed by applicant herein would have been *prima facie* obvious. *Cf., In re Grabiak*, 226 U.S.P.Q. 870 (Fed. Cir. 1985).

Furthermore, the molecular modification of the Zilliken isoflavone derivatives which is required to arrive at the active agents of the present invention cannot be presumed to be obvious from the disclosure of the Zilliken patent, inasmuch as such modification would be clearly contrary to the invention which is the subject of the Zilliken patent, i.e., isoflavone derivatives having an -OR substituent at the 6-position of the structural formula. *Cf., Ex Parte Hartman*, 186 U.S.P.Q. 366 (Bd. Apps. 1974).

Furthermore, the Zilliken patent plainly fails to show or suggest the ratios, dosage amounts and dosage forms called for in applicant's claims 6-9, as well as the pharmaceutical preparation of new claims 36-38.

Inasmuch as the Zilliken patent fails to show or suggest the claimed subject matter as a whole, it necessarily follows that the Zilliken patent does not render applicant's claims 1-9, 21 and 22 *prima facie* obvious. Therefore, no evidence of unusual or unexpected results needs to be presented in this case. *In re Lunsford*, 148 U.S.P.Q. 721 (CCPA 1966).

In summary, the rejection of claims 1-9, 21 and 22 under 35 U.S.C. §103 based on the disclosure of the Zilliken patent is improper and should be withdrawn.

In view of the amendments presented herewith, the Declaration of Dr. Kelly and the foregoing remarks, it is respectfully urged that the objections and rejections set forth in the September 10, 1996 Official Action be withdrawn and that this application be passed to issue, and such action is earnestly solicited.

Respectfully submitted,

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Enclosure: Declaration of Graham Edmund Kelly